

PERIOPERATIVE EVALUATION AND MANAGEMENT OF A PATIENT WITH CONGESTIVE HEART FAILURE

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Case presentation: Male, 57 years old. Until one week before admission had asymptomatic history, no angina or CHF symptoms. In the last week described complaints of upper respiratory symptoms with influenza-like fever.

Risk factors: Dyslipidemia, NIDDM, smoker.

The patient arrived to the ER with severe dyspnea a week after initial symptoms. Extensive anterior wall MI was diagnosed. Echocardiography on arrival: Severe LV dysfunction. Due to hemodynamic instability: low BP & pulmonary edema, IABP was inserted.

Medications: Continuous diuretics infusion, low dose MO, dobutamine and noradrenalin in escalating doses. Worsening renal function was evident: reduced urinary output, creatinine 2.0 & worsening liver function with elevated enzymes. The patient's condition required a semielective intubation & mechanical ventilation.

The patient was taken to the cath lab and underwent coronary angiography revealing totally occluded proximal RCA, significant OM stenosis and 70% occlusion of the left main coronary artery. PA catheter was inserted and the patient underwent a triple coronary CABG with LIMA and two vein grafts. The LV function was still poor, although some improved function was observed by TEE in the septum and inferior wall. Pulmonary pressures seemed to be high by palpation. Weaning from bypass was a challenge, and was supported by his previous medical support, dobutamine and noradrenalin and additional infusion of milrinone and inhaled NO.

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Goals of discussion:

1. Perioperative evaluation of CHF (for coronary and non coronary surgery), current status of guidelines.
2. Brief pathophysiology of CHF
3. Preoperative guidelines for medical therapy for CHF patient
4. Intraoperative management of the failing heart during weaning from bypass
5. New medications on the market.
6. Postoperative management

Patophysiology: Acute heart failure is defined as the rapid onset of symptoms and signs secondary to abnormal cardiac function. Cardiac dysfunction can be related to systolic or diastolic dysfunction, to abnormalities in cardiac rhythm, or to preload or afterload mismatch. The change in LV performance is usually caused by structural injury (AMI), papillary muscle rupture, cardiomyopathy or myocarditis. The Forrester classification (AJC 1977) was adapted to describe whether the HF is characterized by normal or low cardiac index, high or low blood pressure, and with or without pulmonary congestion. The patient then may be described as warm and dry, warm and wet, or cold and dry or cold and wet. Thus, the two important hemodynamic parameters are blood pressure which represents the hemodynamic performance, and the status of hemodynamic congestion. Troponin will indicate cardiac injury, creatinine and BUN renal dysfunction, and hyponatremia the magnitude of neurohormonal activation.

Preoperative evaluation: Although the guidelines for preoperative evaluation of patients with heart disease are abundant, there are only a few words on patients with congestive heart failure. The ACC/AHA 2007 Guidelines on Perioperative Cardiovascular Evaluation and Care for Noncardiac Surgery (Fleisher LA et al. JACC, 2007) only mentions that „heart failure has been identified as being associated with a poorer outcome when noncardiac surgery is performed. Every effort must be made to detect HF by a careful history and physical examination and it is reasonable for patients with dyspnea of unknown origin or patients with current or prior HF to undergo preoperative evaluation of LV function. (*Level of Evidence: C*)". In the Revised Cardiac Risk Index (Lee TH et al, Circulation 1999) CHF is one of the six criteria for prediction of cardiac risk in noncardiac surgery.

Our aims as anesthesiologists in CHF patient management in the perioperative setting are: a. early identification of patients in active CHF state and b. providing best preemptive medical care. The diagnostic task will be performed by reviewing patient's history and his current medications, by

echocardiographic examination or dobutamine stress echocardiography, and by a relatively new bed-side blood test for NT-proBNP.

BNP: The natriuretic peptides counterbalance the effects of the renin angiotensinaldosterone system. They are antagonists to angiotensin II on vascular tone and to aldosterone secretion. ANP and BNP concentrations increase in response to volume expansion and pressure overload of the heart. Plasma levels of NT-proBNP correlate well with the extent of inducible ischemia and are powerful predictors of death in patients with stable CAD and acute coronary syndromes (Mahla E, Anesthesiology 2007). In an editorial on this last article Augoustides J and Fleisher LA (Anesthesiology 2007) have concluded that „We should include serum markers to better predict the subset of high-risk patients who will experience postoperative adverse cardiovascular outcome and that the results from this study beg future investigation in trials that target perioperative interventions based on this marker“.

Dobutamine Stress Echocardiography is an important means for evaluation of HF and in assessing preoperatively myocardial viability. Karagianis SE and Poldermans D (Am J Cardiol 2007) examined 295 patients with poor LV (EF < 35%) who underwent vascular surgery and they conclude that dysfunctional segments that improve after inotropic stimulation, might enhance preoperative risk stratification, and thus, biphasic pattern, i.e. improvement in wall motion with increasing dobutamine and worsening at higher doses, or sustained improvement in DSE might indicate patients with reduced probability of postoperative cardiac events.

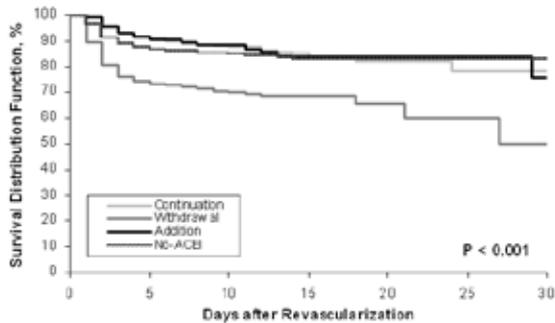
Our second aim is to provide preemptive care, i.e., initiating pharmacological therapy early to improve perioperative outcome by using ACEI, ARB, BB, spironolactone, diuretics, and in acute decompensated situations drugs like dobutamine and milrinone or newer drugs like levosimendan and nesiritide. The preemptive medical care will continue intraoperatively using moderate dosages of anesthetic agents and other drugs (levosimendan) with proven myocardial protection properties.

The angiotensin II – aldosterone – renin hormones are important mediators in the pathogenesis of HF. They have been implicated in excessive accumulation of collagen within the myocardium, leading to diastolic dysfunction, to systolic HF, and eventually to structural cardiac remodeling. Appropriate therapy, mainly based on ACEI and diuretics, might improve myocardial loading conditions under HF circumstances. More recently, the benefits of ACEI cerebrovascular and renovascular protection. Because of these secondary actions of ACEI (endothelial protective effects), there has been a shift in therapeutic approach from the initial pharmacologic-an-

tihypertensive to a therapeutic approach having a biologic (nonhemodynamic) underpinning (Kjøller-Hansen L, J Am Coll Cardiol 2000). The new European Society of Cardiology guidelines for the pharmacological management of CHF (Maggioni AP, Eur Heart J 2005) re-emphasized that ACEI confer considerable, sustained survival benefits in patients with CHF and are associated with reductions in all-cause mortality and disease progression.

Also in the setting of coronary surgery, the continuous use of ACEI is advocated. We have shown (Drenger B et al. Circulation 2012) that patients on ACEI or those in whom ACEI were added postoperatively had better outcome, particularly cardiac and renal, while when the drug was withdrawn, cardiac outcome and mortality were significantly worsened. Wallace (Wallace AW, Anesthesiology. 2010) addressed the consequences of drug withdrawal postoperatively and in a general surgical unit and provided evidence that withdrawal of 'regular' cardiovascular medicines adds to the risk of the surgery and complicates outcomes. We summarized that in our multicenter and multinational study patients undergoing CABG surgery with CPB, continuation of ACEI therapy early after surgery or adding ACEI *de novo* postoperatively can be associated with marked improvement in cardiovascular and renal outcomes. Conversely, a practice of withdrawing of ACEI treatment postoperatively is associated with poor in-hospital fatal and nonfatal outcomes.

Kaplan-Meier survival analysis of event free status by ACEI therapy. The curves show data of 30-day in-hospital composite event free status.



Cumulative Composite Outcome

| | | | | | | | |
|----------------------|---|-----|-----|-----|-----|-----|-----|
| Continuation (n=915) | 0 | 80 | 104 | 111 | 112 | 113 | 113 |
| Withdrawal (n=923) | 0 | 245 | 262 | 265 | 266 | 267 | 268 |
| Addition (n=343) | 0 | 33 | 37 | 41 | 41 | 41 | 42 |
| No-ACEI (n=2043) | 0 | 269 | 289 | 293 | 293 | 293 | 293 |

Characteristics in the 24 Hours after ICU Arrival by ACEI Treatment Groups

| Characteristics | No-ACEI (N=2043) | Addition (N=343) | Continuation (N=915) | Withdrawal (N=923) | P value† | P value‡ | P value§ |
|--|---------------------|---------------------|-------------------------|-----------------------|-------------|-------------|-------------|
| Mean cardiac output in the 24 hours after ICU arrival, L/min | | | | | | | |
| Median | 5.57 | 5.51 | 5.61 | 5.56 | | 0.84 | 0.93 |
| First quartile–Third quartile | 4.75–6.48 | 4.62–6.48 | 4.75–6.60 | 4.76–6.47 | 0.54 | | |
| Mean SBP in the 24 hours after ICU arrival, mmHg | | | | | | | |
| Median | 116.2 | 121.8 | 120.6 | 115.7 | | <0.001 | <0.001 |
| First quartile–Third quartile | 109.3–123.9 | 113.4–130.0 | 112.9–128.4 | 108.7–123.7 | <0.001 | | |
| Intubation time, hour | | | | | | | |
| Median | 13.2 | 16.4 | 15.6 | 15.4 | | <0.001 | 0.36 |
| First quartile–Third quartile | 9.7–18.4 | 12.0–22.7 | 11.5–22.2 | 11.2–21.3 | <0.001 | | |
| 2 or more simultaneous non-routine inotropes on RDOS – no. (%) | 282 (13.8) | 92 (26.8) | 257 (28.1) | 256 (27.7) | | <0.001 | 0.18 |
| Assist device use for low cardiac output or ischemic or angina | 35 (1.7) | 5 (1.5) | 12 (1.3) | 35 (3.8) | 0.31 | 0.92 | <0.001 |
| Intraoperative or on RDOS – no. (%) | | | | | | | |
| Red blood cell transfusion in 24 hours after ICU arrival – no. (%) | 762 (37.3) | 149 (43.3) | 368 (40.2) | 446 (48.3) | | 0.004 | <0.001 |
| | | | | | 0.09 | | |

A new revival came to an old drug, the spironolactone. This aldosterone-receptor blocking drug can slow the progression of left ventricular remodeling and even produce regression of LV hypertrophy and improves myocardial function in patients with hypertensive heart disease, reducing the occurrence of sudden cardiac death in HF patients (Kalidindi SR, Nature Clin Practice, 2007).

Inotropic and vasodilatory therapy: Inotropes (milrinone or dobutamine) may be considered in patients with diminished peripheral perfusion or end organ dysfunction (low output), particularly those with symptomatic hypotension despite adequate filling pressure (Strength of evidence=C) (HFSA Practice Guidelines 2006). In the absence of symptomatic hypotension, IV nitroglycerine, nitroprusside or nesiritide may be considered as an addition to diuretics for rapid improvement of hemodynamic parameters and congestive symptoms in patients admitted with acute decompensated HF (B).

Dobutamine binds to Beta1-adrenergic receptors on the surface of cardiac myocytes. This receptor stimulates the activity of G protein and then activates adenylyl cyclase with conversion of ATP to cAMP. This second messenger activates the cAMP-dependent protein kinase, opening L-type calcium channels, thereby increasing intracellular levels of calcium. Calcium then activates myocyte contraction. Like Dobutamine, Milrinone works through the cAMP pathway. Phosphodiesterase III normally rapidly converts cAMP to AMP, thereby downregulating the signaling through this pathway.

Milrinone inhibits PDE III, leading to higher concentrations of cAMP and subsequently resulting in higher intracellular calcium concentrations. Dobutamine clinical drawbacks are: increased myocardial oxygen consumption and increased frequency of arrhythmias. Milrinone drawbacks are: decreased vascular resistance and hypotension, particularly with renal insufficiency and increased arrhythmias.

Nesiritide - a recombinant human B-type natriuretic peptide is a relatively new drug with vasodilatory, natriuretic and diuretic effects, primarily mediated via natriuretic peptide receptor-A on vascular smooth muscle, endothelium, kidneys and adrenals, but with no direct inotropic effect. Indication for use is acute decompensated heart failure with dyspnea on minimal exertion or at rest. Nesiritide reduces preload and right atrial pressure with rapid reduction in PCWP, faster than glyceryl trinitrate. It reduces afterload resulting in increase in cardiac output, diuresis & natriuresis. In a meta-analysis by Sackner-Bernstein JD, (JAMA. 2005), the short-term risk of death was found to be higher with nesiritide, and as well, the same authors demonstrated a higher risk of worsening renal function with nesiritide in patients with acutely decompensated heart failure (Circulation 2005). An

FDA committee run by E. Braunwald concluded that because of the small number of events in the current database and the inconclusive nature of these findings, the panel recommends that additional studies be conducted to assess the effect of nesiritide on survival.

Levosimendan (Simdax®) – is a calcium sensitizer drug, i.e., is selectively binding to cardiac troponin C, and thus enhances contractility with no change in total intracellular Ca^{2+} . Additional mechanisms of action are opening of sarcolemma KATP channels on vascular smooth-muscle cells, resulting in vasodilation in all vascular beds, and lowering preload and afterload with anti-ischemic effect. Its preconditioning action, i.e., opening of mitochondrial KATP channels in cardiomyocytes produces myocardial protection and anti-apoptosis following ischemia–reperfusion stimulus. (Rapp Z, Drug Rev. 2005), with reduced infarct size in animal studies (Kersten J, Anesth Analg 2000). Most of the available drugs that open KATP channels have an intrinsic negative inotropic effect, mediated by a reduction in the cytosolic calcium transient. The dual mechanism of Levo as calcium sensitizer counterbalance the negative inotropic effect due to PC (Less Ca^{2+} influx but more sensitivity). De Hert SG et al (Anesth Analg 2007) have shown that stroke volume was better maintained with the combination of dobutamine with levosimendan than with the combination of dobutamine with milrinone in cardiac Surgery patients with poor LV function. However, the „SURVIVE“ multicenter study failed to show improvement in 180 days all-cause survival within the levosimendan group. They identified responders and non-responders and concluded that the drug would better be given to acutely decompensated HF patients (NYHA class III-V) with no initial bolus dose and avoid using high doses. Indications for use in low-output syndrome after CPB are in patients manifesting failure-to-wean from CPB (Akgul A, Heart Lung Circ. 2006), and in mitral valve surgery, in case of right ventricular failure after CPB because of low cardiac output and pulmonary hypertension (Morais RJ, JCTVA 2006).

In summary, management of low cardiac output syndrome during open heart surgery should include a comprehensive approach by the anesthetic team which includes: proper monitoring, judicious use of inotropes and diuretics, the use of volatile anesthetics for their myocardial protection properties, and early consideration using a new generation of drugs: nesiritide (pending additional studies to assess its effect on survival) and levosimendan.

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